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Relationship Between Humans and Their Viruses

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I. INTRODUCTION

Many of the viruses that can infect humans should not be considered as viruses of humans, but rather as zoonotic. Zoonotic viruses are those viruses of animals that can cross boundaries such that they occasionally infect humans. Some examples of diseases induced in humans by zoonotic viruses are dengue and Ebola fever, the equine encephalitids (i.e., Eastern, St. Louis, Venezuelan, and Western), hantavirus pneumonia, Lassa fever, Marburg fever, rabies, and yellow fever. Additionally, it should be noted that the zoonotic category includes most, if not all, of the human illnesses induced either by arboviruses (viruses whose transmission is vectored by arthropods) or by the hemorrhagic fever viruses. With respect to the zoonotic viruses humans are, at best, alternate hosts. Humans do in fact usually represent dead-end hosts for these zoonotic viruses, meaning that subsequent transmission of those viruses either to new humans or back to the natural host is not sustained.

There is a subgroup of zoonotic viruses that, although principally remaining viruses of animals, seem to have adapted themselves to use humans as natural hosts. This adaptation is indicated by the fact that these viruses have demonstrated an ability to sustain a chain of transmission among humans. Examples of zoonotic viruses that have shown this ability to adapt themselves to become viruses of humans are those members of the family Flaviviridae (genus *Flavivirus*) that induce the human diseases known as dengue and yellow fever.

All of the above-mentioned zoonotic viruses contrast with the viral agents that clearly are known by their nature to be viruses of humans. Examples of viruses of humans are those that induce the diseases known as acquired immunodeficiency syndrome, fever blisters, measles, mumps, polio, rubella, smallpox, T-cell leukemia, T-cell lymphoma, and type A influenza. The aim of this chapter is to address those viruses that are considered to be viruses of humans. Those viruses of terrestrial mammals that are considered to be zoonotic are addressed by Calisher and Fenner in Chapter 13.

Every virus species needs to have a successful overall approach for sustaining its existence. That overall approach must enable the virus to attain its two principal goals, namely, that the virus be able to reproduce itself within a host and that the virus then be transmitted onward to a new host. Those mechanisms that any given virus species employs for achieving its sustainment, of course, have been developed through a process that involved an initiation of events by random chance followed by evolutionary selection. The most successful overall approaches may be those that subsequently evolve into the types of relationships between a virus and its host species that will allow the virus to persist without eliminating the host population. This latter point is very important, because the virus may in turn become extinct if it kills off the host population. It is for this reason that excessive

virulence will be detrimental to the virus, and an interesting side point may be that, if an individual host cannot successfully surmount the infection, then the death of that individual host may be seen as an altruistic defense mechanism for the host population as a whole.

II. ACHIEVING THE GOAL OF VIRAL REPRODUCTION

Achieving self-reproduction is the first principal goal of the virus. The processes involved can be divided into three aspects. The first aspect is the virus's overall approach with regard to the course of the infection it establishes within the host. This involves the time course of the infection and the extent to which infectious progeny viral particles are produced during the course of the infection. The second aspect is the replication strategy employed by the virus. This involves the issues of where the virus begins its march through the host body and the physical trajectory followed until the virus exits in search of a new host. The third aspect involves which approaches, if any, the virus uses to avoid the host defensive mechanisms.

A. Strategy of the Infection Course

As mentioned in Chapter 1, the goal of establishing an effective course of infection is an aspect of viral reproduction that can be attained in many ways. We can summarize the strategies that viruses use as following four basic patterns.

1. Productive Infections

Three out of the four patterns of the course of viral infection are considered to be productive. The infection will be acquired in the form of infectious viral particles, and subsequently produced progeny viral particles then serve to infect future hosts. Productive, in this context, means that the number of progeny viral particles produced during the course of an infection is sufficient for the particles to transmit the infection to a new host with some reasonable probability. The productive approach involves an evolutionary decision as to whether there will be either a very short initial but highly productive course of infection (short term-initial), a course of infection that is prolonged but only intermittently productive (recurrent), or a productive though very slow course of infection whose severity progressively increases with time to reach a dramatic end-stage (increasing to end-stage). These three patterns can be described as follows.

a. ***Short Term-Initial.*** Viral production only occurs during a short time course near the time of initiation of the infection, which then abruptly ends. The human host may or may not survive beyond the course of this short infection. Host survival depends on the type of virus involved, the extent to which the involved virus and humans have had time to coevolve as species, and whether or not the ancestral humans of that particular subgroup of the human host population previously have had contact with the causative virus. Coevolution usually will tend to make the outcome of this pattern of viral infection sufficiently mild as to be associated with a fairly low incidence of mortality in an otherwise healthy population of human hosts. Some examples of this pattern would be the infections caused by the human caliciviruses (family Caliciviridae), human influenza viruses (family Orthomyxoviridae), human polioviruses and human rhinoviruses (family Picornaviridae), and the human rotaviruses (family Reoviridae).

b. ***Recurrent.*** Viral production, often very pronounced initially, is recurrent when the virus persists in a latent state within the host body and viral particle production periodically recurs but is not life threatening. Some examples of this pattern would be the infections caused by the human herpesviruses (family Herpesviridae) and the human papillomaviruses (family Papovaviridae).

c. ***Increasing to End-Stage.*** Viral infection normally is associated with a slow, almost innocuous, start, followed by a gradual progression, associated with an increasing level of viral production and eventual host death. Death of the host may relate to destruction of host immunological defense systems, which then results in death by secondary infections. This pattern of infection may take from 10 to 40 years to kill a human host. The infections caused by the human immunodeficiency viruses and the human T-lymphotropic viruses (all belonging to the family Retroviridae) represent examples of this pattern.

2. Nonproductive Infections

The fourth basic pattern of viral infection is considered to be nonproductive. A nonproductive infection is one in which the production of infectious virus particles is so limited that the virus must transmit itself through other means, usually by transferring a copy of only the nucleic acid genome of the virus. In these instances, the viral infection is normally acquired by direct transfer of the viral genetic material from the human parents to their developing fetuses, such transfer occurring via the egg and sperm cells. There may be no apparent health effects associated with such an infection. An example of this pattern is the infections caused by the endogenous retroviruses (family Retroviridae), whose genomes are incorporated into the chromosomal material of every cell in the human body (Villareal,

1997). The nonproductive pattern of infection seems to suggest the highest degree of coevolution between a virus and its host, since a nonproductive virus has no means of transmitting itself to a new host without some very active, albeit perhaps unwitting, participation on the part of the present host.

B. Strategy of Viral Replication

This section addresses the questions of where and how the virus begins its march through the host body, and how the virus then continues the course of this attack, leading ultimately to the concept of viral reproduction strategies at the host population level.

1. Cellular Metabolic Level

Discussion of the strategy of viral replication within the body of a host organism begins at the most basic level, which is attachment of the virus to a particular molecule present on the surface of host cells. Such a molecule is said to be the "virus's receptor," and will be some cellular protein or lipid component naturally produced by those cells. The virus's choice of receptor is a product of viral evolution. After binding to its receptor, the virus gains entrance to the interior of the cell and viral replication begins. Viruses whose genomes are composed of DNA generally replicate mainly within the nucleus. In contrast, those viruses with RNA genomes generally focus their center of replication in the cytoplasm. During the course of replication, the virus must decide which cellular systems and machinery it will employ. Some large viruses carry the genomic coding capacity for many of their own enzymes, while others may rely almost completely on the enzymatic machinery possessed by the host cell. Many viruses, including those belonging to the genus *Enterovirus* of the family Picornaviridae, are said to be highly cytopathogenic, meaning that they usually quickly kill the host cell as a result of infection. Other viruses, such as those that occupy the genus *Rubivirus* of the family Togaviridae, may cause prolonged and severe crippling of the cell rather than killing it outright. A further discussion of these issues can be found in Chapter 3.

2. Tissue and Organ Tropism Level

Viruses vary greatly with respect to the tissues they tend to target for infection. On a larger scale, this then leads to identification of those organs that the viruses are affecting. This selective targeting is referred to as a "tropism." Viral tropisms

can be divided into those considered primary and those considered secondary. Primary tropisms will be associated with production of those viral particles that subsequently contribute to transmission of the viral infection to a new host. As such, the primary tropisms tend to be related to those sites (termed "portals") through which the virus either enters or exits the host body. Secondary tropisms may represent accidents. Some of these accidents may come about as a result of the molecule that a virus uses as its receptor, existing on the cells of tissues that are unrelated to those that the virus must employ in order to achieve transmission. Nevertheless, secondary tropisms may contribute greatly to the types and severity of the illnesses associated with infection of humans by any particular virus.

3. Host Population Level

When considered at the host population level, the strategy of viral replication includes the ease with which or likelihood that a virus is transmitted to new hosts plus the severity of infection and accompanying likelihood of death (including the age-related likelihood of death) for any given host individual.

C. Strategies for Evading Host Defensive Mechanisms

Through the course of evolution, many viruses have developed mechanisms for either countering or evading the human immune and non-immune defenses as a means for enhancing the probability of viral success.

1. Avoiding the Host Immune Defenses

The human immune system includes both humoral (antibody-mediated) and cellular components. The cellular components can include granulomatous reactions, which play a role in defense against protozoans, though their possible role in antiviral defenses has been incompletely explored. Those mechanisms that viruses use to either avoid or minimize attack by the host immune system can be divided into the four following groups. The use of these types of mechanisms seems particularly critical in association with those viral infections that persist within a human host for very long periods of time, often up to decades.

a. ***Antigenic Mimicry***. The produced antigens are similar to those of the host, as with prions.

b. ***Rapid Viral Mutation***. This mechanism includes both antigenic drifting and shifting. Some viral types demonstrate rapid viral mutation during the course of an infection, as occurs with the human immunodeficiency viruses of the family Retroviridae. Other virus types, such as the influenza viruses of the family Orthomyxoviridae, demonstrate rapid viral mutation between reinfections of the same host.

c. ***Low Antigenicity***. Some viruses inherently seem to provoke little, if any, immune response. This often occurs because the virus persists in a latent state within host cells, during which time either little or no viral antigenic material is produced. Examples include the endogenous retroviruses of the family Retroviridae and the human herpesviruses of the family Herpesviridae.

d. ***Infect the Immune Cells!*** The most direct attack may be the most effective. Exceptionally notorious examples of this approach are the genus *Rubivirus* of the family Togaviridae and the genus *Lentivirus* of Retroviridae.

Aside from the above groupings, some viruses such as the Norwalk virus of the family Caliciviridae seem to be antigenic but provoke an immune response that is minimally effective.

2. Avoiding the Host Non-Immune Defenses

The body has non-immune defense mechanisms that help to protect against viral infections. These mechanisms are associated with the portals through which viruses can enter the body of a host. Examples of non-immune defenses include the enzymes secreted as a part of pancreatic fluid, saliva, and tears. Various glands associated with mucosal tissues secrete antimicrobial compounds into the mucus produced by those tissues. Some mucosal tissues also possess cilia whose movement helps to expel both the mucus and any foreign materials, including pathogens, that become entrapped within the mucus. An additional example of a non-immune defense is the stomach acid produced to aid digestion of organic compounds. Many gastroenteritis viruses, such as the rotaviruses of the family Reoviridae and the astroviruses of Astroviridae, have evolved such an effective resistance to attack by proteolytic enzymes that those viruses virtually need partial proteolysis to facilitate their infectivity. The influenza viruses of the family Orthomyxoviridae are known for their ability to paralyze the activity of the mucosal cilia located within the respiratory tract. One of the defining characteristics for the enteroviruses of the family Picornaviridae is their resistance to acidic exposure.

III. ACHIEVING THE GOAL OF VIRAL TRANSMISSION BETWEEN HOSTS

The task of achieving viral transmission between hosting individuals involves two aspects. The first is the type of infectious material in which a virus will leave its present host, while the second involves the route by which the virus can encounter its proximate host.

A. Type of Infectious Bodily Material in Which Virus Is Released from the Host

The types of bodily materials within which viruses can be released include substances that exit during the course of normal body functions. Among these substances are feces and a variety of liquids, including menstrual blood, respiratory secretions of the upper and lower tracts, saliva, semen, tears, urine, and vaginal fluid. Sweat is another fluid that is naturally released from the body; however, it is not known to contain viruses. Viruses can also be found in blood released from wounds in the skin; from blood acquired by blood-consuming parasitic insects, among which are the fleas and several groups of flies, ticks, and mosquitoes; and blood leaked from swollen or ruptured capillaries into mucosal tissue and skin pores.

B. Route of Transmission between Hosts

Those natural routes by which viruses are transferred to and between humans are the same routes associated with all surface-dwelling terrestrial vertebrates. These routes are tightly associated with the portals of entry and exit that any particular virus family uses as it tries to survive and find its way from one host to the next. Viral transmission routes can be subdivided into two broad groups. The first is transmission by direct contact (also known as direct transfer) between two members of those species that host the virus. This includes both the possibility of transmission between two members of the principal host species and the possibility of transmission between a member of that principal host species and some

alternate host species, and the latter may represent a vectoring species. The second group is transmission by indirect contact (also known as indirect transfer). These routes have been described in detail by Hurst and Murphy (1996) and are represented in Figures 9 and 12 of Chapter 1 herein. As explained in Chapter 1, there are some routes of viral transmission that are considered unnatural vehicular routes. Such routes represent the use of unnatural vehicles as a means to evade the host defenses associated with natural portals of entry. These unnatural routes involve invasive medical devices (such as syringes, endoscopes, and other surgical instruments) and transplanted tissues, including transfused blood and blood products. The remainder of this section describes the natural routes of viral transmission between hosts.

1. Direct Contact

The direct contact approach offers one major advantage and one major drawback to the virus. The advantage is that those viruses transmitted by direct contact need not be stable when exposed to ambient environments. The drawback is that the number of new hosts to which they have potential access may be smaller than for viruses transmitted by indirect contact. Viruses that are endogenous by their nature will survive for as long as the host survives. Although endogenous viruses can only be transmitted to host progeny, these viruses neither have to adapt themselves to nor coevolve with any other hosting species. An example of this type of endogenous agent would be the endogenous retroviruses of the family Retroviridae. Viruses that are venereal in nature, that is, transmitted in semen and vaginal secretions during sexual activity, have a somewhat greater potential for contacting new hosts. Represented among the venereal viruses of humans are some species of the genera *Simplexvirus* (family Herpesviridae) and *Papillomavirus* (family Papovaviridae). Once these venereal viruses infect a host, they remain associated with the host for the rest of the host's life in the form of a permanent infection. Thus, although the frequency with which endogenous and venereal viruses can find a new host is restricted, the viruses compensate for this to some degree by remaining with the host for a very long time. The next step on the scale of host access is represented by those viruses transmitted via direct contact with insect vectors. These viruses have greatly increased access to new hosts and tend not to remain with their present host for the remainder of the host's life. Those viruses transmitted by biting insects are commonly referred to as "arboviruses," which is an abbreviation of "***ar***thropod-***bo***rne ***viruses***." Included among those arboviruses that infect humans are members of the genera *Alphavirus* (family Togaviridae); *Bunyavirus*, *Nairovirus*, and *Phlebovirus* (all of the family Bunyaviridae); and *Flavivirus* (family Flaviviridae).

Viruses transmitted by way of saliva may be perceived as bridging the categories of direct and indirect contact. If any particular type of virus that is secreted into saliva has either no stability when exposed to ambient environments in oral secretions or only limited stability under those conditions, then the virus will have to be transmitted by saliva that is transferred during oral contact between hosts. Conversely, if the particular virus type has good stability when exposed to ambient environments in oral secretions, then that virus can be transmitted on shared food or in association with fomites. Some of the viruses transmitted in saliva do remain associated with the host as a permanent infection, and these often are the viruses that possess limited stability in ambient environments, such as members of the family Herpesviridae. Many of the viruses that are secreted into saliva and can be transferred to a new host in association with fomites do not remain associated with the host as a permanent infection, such as members of the family Picornaviridae. In general, those viruses transmitted by indirect contact between hosting individuals tend to produce only transient infections of their individual hosts rather than remain associated with the individual host as a permanent infection. These several latter points suggest that there may be some evolutionary relationship between ease of viral transmission to a new potential host individual or the frequency of opportunities for viral transmission, and the length of time that a virus must be capable of remaining with its present host to have a reasonable chance of achieving eventual transmission.

2. Indirect Contact (Vehicle-Borne)

The indirect contact approach also offers one major advantage and one major drawback to a virus. Viruses transmitted by indirect contact have the advantage of potential access to a far greater number of hosting individuals than is the case for viruses transmitted by direct contact. The drawback is that the viruses must have evolved stability when they are exposed to the ambient environment. The vehicles that viruses utilize to achieve transmission between hosting individuals by indirect contact are subdivided into the following four categories: food, water, air (in actuality, this refers to aerosols), and fomites. Transmission by any of these four categories of vehicles will usually be associated with some specific physical activity on the part of the present host, and will always be associated with some physical activity on the part of the proximate host.

Of course, foods are items intentionally ingested for their caloric or nutritional value. Food contamination can occur by way of the food being a virally infected animal consumed by the proximate host. In such cases, there is no specific physical activity on the part of the present host (the one being eaten) that can be identified

as having caused the proximate host to be ingesting contaminated food (indeed, perhaps it is a lack of physical activity on the part of the present host that is to blame). Otherwise, viral contamination of foods can result from fecal material being transferred via contact with unwashed hands or if contaminated aerosols fall into the food. A particularly notable example of a virus of humans that is transmitted via foods is the hepatitis A virus of the genus *Hepatovirus* (family Picornaviridae).

Water usually serves as a vehicle after it has been contaminated with fecal material. Acquisition of a viral infection from water usually results from the proximate host ingesting contaminated water. Physical contact of the skin or mucosa of the proximate host with contaminated water, as may occur during recreational activities or body washing, can result in acquisition of infection. Notable examples of viruses transmitted by these waterborne routes are those belonging to the viral families Astroviridae and Caliciviridae, and the genera *Enterovirus* and *Hepatovirus* of the family Picornaviridae.

Viral contamination of air can occur by two principal mechanisms. The first, and most significant, involves release of aerosols that contain droplets of respiratory secretions (i.e., nasal, oral, or pulmonary mucus). This type of transmission route is referred to as being the route of droplet aerosols. Notable examples of viruses transmitted in this manner are those belonging to the viral families Coronaviridae, Orthomyxoviridae, and Paramyxoviridae, and members of the genus *Rhinovirus* of the family Picornaviridae. The second mechanism is by way of particulate aerosols. This involves generation of aerosols composed of soil particles coated with dried urine or feces. Notable examples of viruses transmitted by this route belong to the genera *Arenavirus* (family Arenaviridae) or *Hantavirus* (family Bunyaviridae).

Viral contamination of fomites (defined as solid environmental surfaces that can serve in transmission of infections) can occur in many ways. The variety of things that represent fomites include items used to conserve warmth (e.g., blankets, clothing), items used while eating (e.g., cups, dinner plates, and utensils), tables on which diapers are changed, doorknobs, medical devices, toilet seats, and toys. The ways by which these environmental items become contaminated include projection of droplet aerosols onto environmental objects during sneezing or coughing, aerosols falling onto objects, and unintended surface contamination (including children's clothing, blankets and toys) by blood, feces, fluid from skin lesions (rashes), nasal secretions, saliva, or urine. The task of achieving viral transmission via this route is accomplished when these objects are subsequently handled or used by a potential proximate host. Among the viral genera whose members can be transmitted via fomites are *Orthopoxvirus* (family Poxviridae) and *Rhinovirus* (family Picornaviridae).

IV. SUMMARY OF VIRAL FAMILIES THAT AFFLICT HUMANS

Twenty of the viral families contain members capable of infecting humans. Together, they cause a broad range of illnesses in humans. The terminology used in describing these illnesses is given in Table I. The rest of this section summarizes the ecology of these viral families. Figure 1 schematizes the manner in which the different aspects of the ecology of viral infection fit together. The literature sources used for to compile this summary include Hurst and Murphy (1996), ICTV (1995), Evans and Kaslow (1997), and White and Fenner (1994).

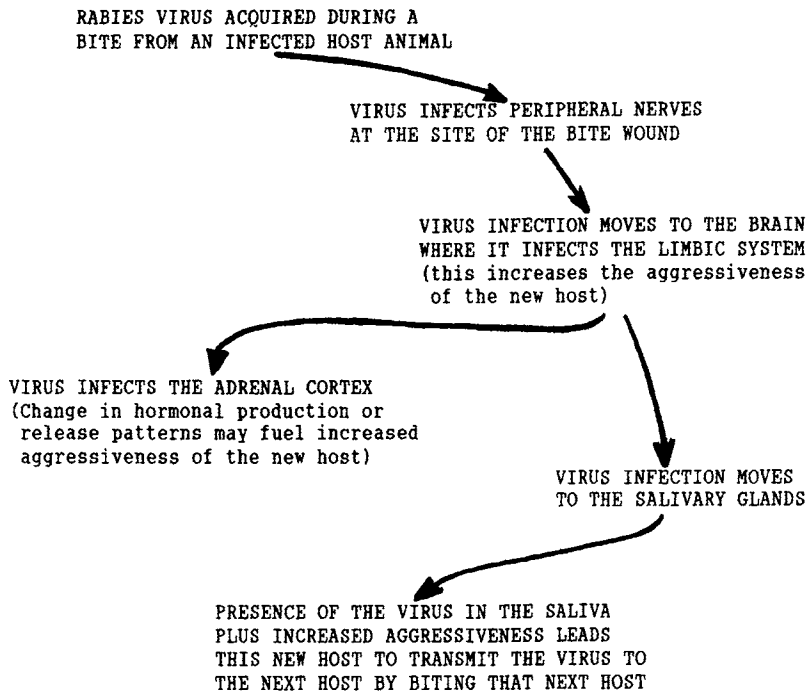

Fig. 1. This figure shows the viral ecology of rabies virus (genus *Lyssavirus*, family Rhabdoviridae) in association with a natural host. Transmission of this virus between hosts occurs when an infected animal bites an uninfected animal, with the virus being transferred by saliva into the bite wound. Subsequent movement of viral infection into the nervous system and salivary glands of the newly bitten host animal is considered to represent primary tropisms, as infection at these sites is directly related to movement of virus into the body of the current host and subsequent transfer of virus to the next host. Infection of the adrenal cortex is considered a secondary tropism, since those viruses produced in the adrenal cortex will not be transferred to a subsequent host animal. However, infection of the adrenal cortex may play a role in the viral ecology by augmenting the aggressiveness of this newly infected host, thereby increasing the likelihood that this animal will then bite other potential host animals.

TABLE I

Terminology of Human Illnesses Induced by Viruses

Term	Definition
Acquired immunodeficiency syndrome	Syndrome of frequent and chronic infections caused by opportunistic pathogens resulting from immunodepletion
Adenopathy	Physiological changes associated with degeneration of adenoid tissues
Anemia	Low iron level in the blood
Arthralgia	Pain in skeletal joints
Arthritis	Syndrome associated with pain and swelling in skeletal joints
Auditory	Related to hearing
Broncheolitis (bronchitis)	Syndrome associated with swelling or related dysfunction of bronchiole tissues
Carcinoma	Tumor of epithelial tissues
Cardiological	Relating to the heart
Carditis	Syndrome associated with swelling or the related dysfunction of heart tissues
Conjunctivitis	Swelling and reddening of the conjunctiva (the mucosal membranes that line the eyelids)
Coryza	Watery discharge from eyes and nose
Diabetes	Syndrome associated with underproduction or dysfunctional use of insulin
Diabetic	A person who has diabetes or some health characteristic related to diabetes
Encephalitis	Syndrome associated with swelling or the related dysfunction of brain tissues
Encephalomyelitis	Syndrome associated with swelling or the related dysfunction of brain and spinal cord tissues
Encephalopathy	Physiological changes associated with degeneration of brain tissues
Encephalopathy, demyelinating	Encephalopathy associated with the myelin tissue that surrounds nerve cells
Edema	Swelling
Encephalitic	Relating to the brain
Enteritis	Syndrome associated with swelling or the related dysfunction of intestinal tissues, frequently evidenced as diarrhea
Erythema	Form of macular rash showing diffused redness of the skin

continued

Term	Definition
Exanthema	Skin rash
Facial	Relating to the face
Fetal	Relating to the fetus
Fetal developmental abnormalities	Defects occurring during development of the fetus
Fetal loss	Spontaneous abortion
Gastritis	Syndrome associated with swelling or the related dysfunction of stomach tissues, frequently evidenced as vomiting
Gastroenteritis	Combined syndrome of gastritis and enteritis, frequently evidenced as vomiting and diarrhea
Hematemesis	Vomiting of blood
Hematuria	Blood in the urine
Hemolytic uremia	Syndrome consisting of hemolytic anemia (anemia due to blood cell lysis), a reduced level of thrombocytes, and acute degeneration of kidney tissues
Hemorrhagic fever	Syndrome consisting of massive hemorrhage and high fever
Hepatic	Relating to the liver
Hepatitis	Syndrome associated with swelling or the related dysfunction of liver tissues
Hepatomegaly	Enlargement of the liver
Immunodepletion	Reduced level of circulating immune cells
Immunosuppression	Suppressed functioning of the immune system
Keratoconjunctivitis	Combined syndrome associated with swelling or the related dysfunction of both the cornea and conjunctiva tissues
Leukemia	Cancerous syndrome associated with an extremely high level of circulating white cells in the blood
Lymphoma	Solid tumor of the immune system
Malaise	Syndrome characterized by an extremely low level of motivational energy
Malignancy	A spreading cancer
Melena	Bleeding into the lumen of the intestines evidenced by the voiding of tarlike fecal material

continued

Term	Definition
Meningitis	Syndrome associated with swelling or the related dysfunction of meningeal tissues (membranes that enclose the brain and spinal cord)
Meningoencephalitis	Combined syndrome of encephalitis with meningitis
Mucosa	Tissues that secrete mucus
Myalgia	Tenderness or pain in the muscles
Myelopathy	Physiological changes associated with degeneration of the spinal cord
Myocarditis	Syndrome associated with swelling or the related dysfunction of heart tissues
Myositis	Syndrome associated with swelling or the related dysfunction of muscle tissues
Nasopharyngitis	Combined syndrome associated with swelling or the related dysfunction of both the nasal passage and pharynx tissues
Necrosis	Death of tissue cells
Necrotic lesion	Focal area of tissue cell death
Nerve deafness	Loss of hearing resulting from reduced functioning of nerve cells
Neuralgia	Severe sharp pain along the course of a nerve
Neuronal	Relating to the nerve cells
Nodule	A small knotlike protuberance or swelling of tissue
Orchitis	Syndrome associated with swelling or the related dysfunction of testicular tissues
Otitis media	Syndrome associated with swelling or the related dysfunction of middle ear tissues
Paralysis	Loss of mobility
Pericarditis	Syndrome associated with swelling or the related dysfunction of pericardial tissues (fibrous membrane sack that enfolds the heart)
Pharyngitis	Syndrome associated with swelling or the related dysfunction of the pharynx tissues
Pharyngoconjunctival fever	Combined syndrome of conjunctivitis and pharyngitis with fever
Pneumonia	Syndrome associated with swelling or the related dysfunction of lung tissues (by definition, this term indicates that the swelling was induced by an infection)

continued

Term	Definition
Pneumonia, hemorrhagic	Pneumonia accompanied by bleeding into the lungs
Pneumonitis	Syndrome associated with swelling or the related dysfunction of lung tissues (by definition, this term indicates that the swelling was induced by an unknown irritation)
Rash, hemorrhagic (petechial)	Bleeding within the skin evidenced by purple spots termed petechiae
Rash, macular	Discolored spots of various size and shape on the skin (or on the mucosa) that are neither elevated nor depressed
Rash, maculopapular	The presence of both macules and papules on the skin or mucosa
Rash, papular	Small, red circular elevated solid areas on the skin (or on mucosa) that may progress to become either vesicles (filled with clear liquid) or pustules (filled with pus), or may first fill with clear liquid and then with pus
Renal dysfunction	Dysfunction of the kidneys
Retinitis	Syndrome associated with swelling or the related dysfunction of the retina
Retroocular pain	Pain centered behind the eyeball
Salivary glands	Glands that produce saliva
Sarcoma	Cancer arising from connective tissue such as muscle or bone
Sinusitis	Syndrome associated with swelling or the related dysfunction of nasal sinus tissues
Splenomegaly	Enlargement of the spleen
Tracheobronchitis	Syndrome associated with swelling or the related dysfunction of both trachea and bronchiole tissues
Trimester	One third of a time period; usually refers to either the first, second, or third 3-month segment of the 9-month human fetal gestation period
Tumor	Solid abnormal growth of cells
Visual	Relating to vision

A. Viral Family Adenoviridae

Genus affecting humans: *Mastadenovirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Species affecting humans seem naturally limited to humans.

Types of illnesses induced in humans: Adenopathy (the origin of the family name), conjunctivitis, coryza, encephalitis, gastroenteritis, keratoconjunctivitis, pharyngitis, pharyngoconjunctival fever, and pneumonia.

Familial strategies:

Infection course — productive, both short term-initial and recurrent.

Viral replication — at the individual host level, the primary tissue and organ tropisms are toward the cervix, conjunctiva, pharynx, small intestine, and urethra; the secondary tissue and organ tropisms are toward the brain, kidney, lungs, and lymph nodes; at the host population level, these viruses generally are endemic and initially acquired at a very early age, with the infections very often asymptomatic in young children.

Evasion of host defenses — uncertain.

Predominant routes of transmission between hosts: Direct contact via host-to-host and indirect (vehicle-borne) contact via fecally contaminated water, food, fomites, and fomites contaminated by respiratory secretions.

B. Viral Family Arenaviridae

Genus affecting humans: *Arenavirus*.

Familial nature with respect to members affecting humans: Zoonotic.

Natural hosts: Rodents, including commensal voles and mice, as well as commercial colonies of hamsters and nude mice.

Types of illnesses induced in humans: Arthralgia, carditis, encephalomyelitis, encephalopathy, facial edema, fetal loss, focal necrosis of liver, gastritis, hemorrhagic fever, hepatitis, inhibition of platelet function (causes the fatal bleeding associated with this virus family), malaise, meningitis, myalgia, nerve deafness, and pneumonia.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, the primary tissue and organ tropisms presumably are toward the liver and lungs; the secondary tissue and

organ tropisms are toward the brain, fetus, heart, joints, and nerves; at the host population level, these viruses can be extremely devastating to individual hosts but are poorly transferred between humans, which usually represent dead-end hosts.

Evasion of host defenses — uncertain.

Predominant routes of transmission between hosts: Indirect (vehicle-borne) contact via inhalation of particulate aerosols bearing dried rodent urine or acquisition of infectious materials through skin abrasion (a form of surface contact).

C. Viral Family Astroviridae

Genus affecting humans: *Astrovirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Species affecting humans seem naturally limited to humans.

Types of illnesses induced in humans: Enteritis, gastroenteritis.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, the primary tissue and organ tropisms are toward the small intestine; the secondary tissue and organ tropisms presently are unknown; at the host population level, these viruses are endemic, principally causing a mild enteritis seen in young adults.

Evasion of host defenses — avoids host non-immune defenses by resistance to proteolytic attack (their infectivity is actually increased by proteolytic attack).

Predominant routes of transmission between hosts: Indirect (vehicle-borne) contact via fecally contaminated water, food, and fomites.

D. Viral Family Bunyaviridae

Genera affecting humans: *Bunyavirus*, *Hantavirus*, *Nairovirus*, *Phlebovirus*.

Familial nature with respect to members affecting humans: Zoonotic.

Natural hosts: Largely rodents, but also hares and rabbits, and some ungulates.

Types of illnesses induced in humans: Arthralgia, encephalitis, hematemesis, hematuria, hemolytic uremia, hemorrhagic fever, hemorrhagic pneumonia, hemorrhagic (petechial) skin rash, hepatitis, melena, myalgia, pneumonia, renal dysfunction, retinitis, retroocular pain.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, the primary tissue and organ tropisms are toward the kidneys, liver, and lungs; the secondary tissue and organ tropisms are toward the brain and eyes; at the host population level, these viruses are not well sustained within human populations, and humans usually represent dead-end hosts.

Evasion of host defenses — uncertain, but may include avoiding host immune defenses by infecting immune cells.

Predominant routes of transmission between hosts: Direct host-to-vector contact by gnats, midges, mosquitoes, sandflies, and ticks for the genera *Bunyavirus*, *Nairovirus*, and *Phlebovirus*, and indirect (vehicle-borne) contact via particulate aerosols containing dried rodent urine, or contact with rodent excreta or contaminated fomites for the genus *Hantavirus*.

E. Viral Family Caliciviridae

Genus affecting humans: *Calicivirus*.

Familial nature with respect to members affecting humans: Viruses of humans and zoonotic.

Natural or alternate hosts: Fish, terrestrial as well as marine mammals (especially swine).

Types of illnesses induced in humans: Gastroenteritis, hepatitis (nonprogressive, but extraordinarily high fatality rate — 10 to >25% — for women if contracted during the third trimester of pregnancy), myalgia.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the small intestine; secondary tissue and organ tropisms are toward the liver; at the host population level, these tend to be epidemic within human populations; for the hepatitis E virus it seems that acquisition occurs from swine, with the result being epidemics (often very widespread) of human disease; some acquisition from animals may come from eating infected animals; subsequent transmission of all caliciviruses within human populations is by fecally contaminated waste and thus can be very widespread.

Evasion of host defenses — avoids host non-immune defenses by resistance to proteolytic attack.

Predominant routes of transmission between hosts: Indirect (vehicle-borne) contact via fecally contaminated water, food, and fomites.

F. Viral Family Coronaviridae

Genera affecting humans: *Coronavirus*, *Torovirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Some terrestrial ungulates and carnivores.

Types of illnesses induced in humans: Coryza, gastroenteritis.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, the primary tissue and organ tropisms are toward the intestines, lungs (possibly), nasopharynx, and sinuses; at the host population level, these viruses are very widespread and essentially nonfatal.

Evasion of host defenses — avoids host immune defenses by viral mutation and recombination.

Predominant routes of transmission between hosts: Indirect (vehicle-borne) contact via fecally contaminated water, food, and fomites.

G. Viral Family Filoviridae

Genus affecting humans: *Filovirus*.

Familial nature with respect to members affecting humans: Generally zoonotic.

Natural hosts: Unknown, but may include bats and rodents, with primates serving as intermediary hosts leading to human exposure.

Types of illnesses induced in humans: Conjunctivitis, hemorrhagic fever (frequently fatal, death possibly resulting from extreme inflammatory response), hepatic necrosis, myalgia, pharyngitis.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the immune cells and liver (possibly); secondary tissue and organ tropisms are toward the adrenal glands, kidneys, liver, and spleen; at the host population level, these viruses are transferred between humans but seem unable to be sustained in human populations; humans usually represent dead-end hosts.

Evasion of host defenses — avoids host immune defenses by infecting immune cells.

Predominant routes of transmission between hosts: Direct contact via host-to-host transfer of contaminated bodily fluids.

H. Viral Family Flaviviridae

Genera affecting humans: *Flavivirus*, *Hepatitis C-like viruses*.

Familial nature with respect to members affecting humans: Viruses of humans and zoonotic.

Natural or alternate hosts: Members of the genus *Flavivirus* cross-infect a variety of birds and terrestrial mammals via mosquitoes or ticks (depending on the viral species) and most clearly are zoonotic, although those that cause yellow fever and the four that cause dengue may have become viruses of humans without time to coevolve; one species of the genus *Hepatitis C-like viruses* affects humans and seems naturally limited to humans.

Types of illnesses induced in humans: Arthritis with rash, encephalitis, hemorrhagic fever, hepatitis (chronic, which may lead to hepatocellular carcinoma).

Familial strategies:

Infection course — short term-initial for the genus *Flavivirus*, increasing to end-stage for the hepatitis C virus.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the immune cells (principally monocytes and macrophages) and liver; secondary tissue and organ tropisms are toward the brain and liver; at the host population level, most of these viruses are zoonotic, with humans representing dead-end hosts; however, some can be sustained within human populations and occasionally have high lethality rates.

Evasion of host defenses — avoids host immune defenses by infecting immune cells.

Predominant routes of transmission between hosts: For flaviviruses, direct host-to-vector contact; for hepatitis C virus, presumably direct contact via host-to-host transfer of contaminated bodily fluids.

I. Viral Family Hepadnaviridae (and Genus *Deltavirus*)

Genera affecting humans: *Orthohepadnavirus*. The hepatitis D virus (HDV) is a member of the floating genus *Deltavirus*; it is a defective satellite virus which can coinfect humans, but only in association with the hepatitis B virus (HBV) because HDV encapsidates itself with proteins encoded by the genome of the coinfecting HBV.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: One species of viral family Hepadnaviridae (hepatitis B virus) is known to infect humans, and it seems naturally limited to humans.

Type of illness induced in humans: Hepatitis, which may become chronic in adults.

Familial strategies:

Infection course — productive, short term-initial, and increasing to end-stage.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the liver; secondary tissue and organ tropisms are toward the bile duct epithelium, circulating immune cells, and pancreatic acinar cells; at the host population level, when acquired by adults and older children, these viruses generally cause an acute but short-term illness that sometimes can be fulminant; when acquired by neonates or younger children, initially tends to be subclinical but becomes chronic, and the tendency to be chronic can be racially associated (Chinese, possibly also Black African).

Evasion of host defenses — avoids host immune defenses by infecting immune cells.

Predominant routes of transmission between hosts: Direct contact via host-to-host transfer of contaminated bodily fluids and perinatally from contaminated maternal blood.

J. Viral Family Herpesviridae

Genera affecting humans: *Cytomegalovirus*, *Lymphocryptovirus*, *Roseolovirus*, *Simplexvirus*, *Varicellovirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Species affecting humans seem naturally limited to humans, but may pass to primates.

Types of illnesses induced in humans: Carcinoma, carditis, chronic gastrointestinal infection, encephalitis, hepatomegaly, keratoconjunctivitis, lymphoma, myelitis, neuralgia, papular rash of skin and mucosa, paralysis, retinitis, splenomegaly.

Familial strategies:

Infection course — productive, recurrent.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the genital and oral mucosa, pharynx, and salivary glands; secondary tissue and organ tropisms are toward the eyes, kidneys, liver, lymph nodes, nervous system including brain, and spleen; at the host population level, these viruses are ubiquitous, tend to be acquired in childhood or early adulthood, and seldom directly result in host death.

Evasion of host defenses — avoids host immune defenses by infecting immune cells.

Predominant routes of transmission between hosts: Direct contact via host-to-host transfer of fluid from viral-induced lesions of skin or mucosa and by saliva contaminated by chronically infected salivary glands; plus transmission to offspring either transplacentally, intrapartum (during the birth process), or via breast milk.

K. Viral Family Orthomyxoviridae

Genera affecting humans: *Influenzavirus A*, *Influenzavirus B*, and *Influenzavirus C*.

Familial nature with respect to members affecting humans: Generally viruses of humans.

Alternate hosts: Birds (possibly), swine.

Types of illnesses induced in humans: Coryza, malaise, myalgia, nasopharyngitis, pneumonia, retroocular pain, tracheobronchitis.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the ciliated columnar epithelium of the respiratory tract (the exact tissue tropism is directly related to the virus hemagglutinin [HA] serotype); at the host population level, these viruses constantly undergo antigenic drift and antigenic shift and cause wide-scale seasonal epidemics in humans, although infection-related fatality is usually limited to humans aged 65 or older (most notably, age 75 or older).

Evasion of host defenses — avoids host immune defenses by antigenic mimicry and by rapid viral mutation.

Predominant routes of transmission between hosts: Indirect (vehicle-borne) contact via droplet aerosols (from sneezing and coughing) and aerosol-contaminated fomites.

L. Viral Family Papovaviridae

Genera affecting humans: *Papillomavirus*, *Polyomavirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Species affecting humans seem naturally limited to humans.

Types of illnesses induced in humans: Benign tumors of skin and mucosa that may progress to malignancy, progressive demyelinating encephalopathy.

Familial strategies:

Infection course — productive, recurrent.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the mucosa and skin (genus *Papillomavirus*) and toward the upper respiratory tract (genus *Polyomavirus*); secondary tissue and organ tropisms are toward the brain and kidneys (genus *Polyomavirus*); at the host population level, these viruses are ubiquitous and almost never directly responsible for host death.

Evasion of host defenses — avoids host immune defenses by antigenic mimicry.

Predominant routes of transmission between hosts: Presumably direct contact via host-to-host or indirect (vehicle-borne) contact by way of fomites (genus *Papillomavirus*); indirect (vehicle-borne) contact via aerosols (genus *Polyomavirus*).

M. Viral Family Paramyxoviridae

Genera affecting humans: *Morbillivirus*, *Paramyxovirus*, *Pneumovirus*, *Rubulavirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Species affecting humans seem naturally limited to humans.

Types of illnesses induced in humans: Bronchiolitis, conjunctivitis, coryza, encephalitis, glandular enlargement (especially salivary glands), immunosuppression (*Morbillivirus* causes an immunosuppression that is temporary, but which is arguably the most severe induced by a virus of humans, and can result in death by other coinfecting pathogens, such as enteric protozoans, that normally would not cause fatality), macular rash, nerve deafness, orchitis, pneumonitis.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the epidermis and mucosa (including conjunctival, oral and respiratory); secondary tissue and organ tropisms are toward the brain, breasts, circulating immune cells, and testicles; at the host population level, these viruses tend to be acquired at a young age and are almost never directly responsible for host death, although severe sequelae can result if acquired beyond early childhood.

Evasion of host defenses — avoids host immune defenses by infecting immune cells.

Predominant routes of transmission between hosts: Indirect (vehicle-borne) contact via aerosols.

N. Viral Family Parvoviridae

Genus affecting humans: *Parvovirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Species affecting humans seem naturally limited to humans.

Types of illnesses induced in humans: Anemia, arthralgia, erythema, myalgia.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the throat; secondary tissue and organ tropisms are toward the circulatory system, erythrocyte precursor cells in bone marrow, possibly reticulocytes in blood, and skin; at the host population level, these viruses usually cause a disease of childhood; parvoviral disease is either mild or self-limiting in otherwise healthy children or adults.

Evasion of host defenses — uncertain.

Predominant routes of transmission between hosts: Uncertain, but potentially direct host-to-host contact, including transplacental, and indirect (vehicle-borne) contact via aerosols and fecally contaminated water, food, and fomites.

O. Viral Family Picornaviridae

Genera affecting humans: *Enterovirus*, *Hepatovirus*, *Rhinovirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Species affecting humans seem naturally limited to humans, but may pass to primates and canines.

Types of illnesses induced in humans: Diabetes, encephalitis, macular and maculopapular rashes of skin and mucosa, meningitis, myocarditis, otitis media, paralysis of skeletal muscles (occasionally including the diaphragm), pericarditis, retroocular pain, sinusitis (genus *Enterovirus*); hepatitis (nonprogressive) (genus *Hepatovirus*); coryza (genus *Rhinovirus*).

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the nasopharynx and small intestine; secondary tissue and organ tropisms are very genus and species specific and toward the beta cells of the pancreas, conjunctiva, liver, meninges, muscles (including the heart), neurons (including those of the central nervous system), and skin; at the host population level, infections caused by members of the genus *Enterovirus* usually are nonfatal, and both *Enterovirus* and *Hepatovirus* tend to result in asymptomatic

infections if acquired in infancy, though the likelihood of severe symptomatology increases with age at acquisition; infections caused by members of the genus *Rhinovirus* generally are symptomatic but essentially nonfatal regardless of host age.

Evasion of host defenses — members of genus *Enterovirus* avoid host non-immune defenses by resistance to low pH (resistant to stomach acid) and to moderate alkalinity.

Predominant routes of transmission between hosts: Indirect (vehicle-borne) contact via aerosols and fecally contaminated water, food, and fomites.

P. Viral Family Poxviridae

Genera affecting humans: *Molluscipoxvirus*, *Orthopoxvirus*, *Parapoxvirus*.

Familial nature with respect to members affecting humans: Viruses of humans and zoonotic.

Alternate hosts: One species affecting humans (smallpox) seems naturally limited to humans; monkeypox is a very notable but rare zoonotic exception and is presumably acquired from monkeys; several other species may cycle with domesticated bovines and ovines appearing as lesions on teats and udder.

Types of illnesses induced in humans: Necrotic lesions of abdominal organs and skin, nodules and tumors in skin, papular rash.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the skin; secondary tissue and organ tropisms are toward the internal organs and lymph nodes; at the host population level, these viruses have very low transmissibility but have prolonged survivability on fomites due to extreme resistance to desiccation.

Evasion of host defenses — avoids host immune defenses by antigenic mimicry.

Predominant routes of transmission between hosts: Direct contact via host-to-host contact with skin lesions and indirect (vehicle-borne) contact via lesion-contaminated fomites (very notably blankets and other bedding items).

Q. Viral Family Reoviridae

Genera affecting humans: *Coltivirus*, *Orthoreovirus*, *Rotavirus*.

Familial nature with respect to members affecting humans: Viruses of humans and zoonotic.

Natural or alternate hosts: Those species of the genus *Coltivirus* infecting humans seem zoonotic with terrestrial mammals (notably rodents and squirrels) serving as their natural hosts; species of the genus *Orthoreovirus* cross-infect nearly all known terrestrial mammals (especially rodents); those species of the genus *Rotavirus* affecting humans seem naturally limited to humans.

Types of illnesses induced in humans: Hemorrhagic fever, meningoencephalitis (genus *Coltivirus*); upper respiratory symptoms (possibly associated with genus *Orthoreovirus*); gastroenteritis (genus *Rotavirus*).

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are highly genus specific, and are toward the immune cells (genus *Coltavirus*), possibly upper respiratory area (genus *Orthoreovirus*), and the small intestine (genus *Rotavirus*); secondary tissue and organ tropisms are toward the brain and meninges; at the host population level, these viruses have high transmissibility, especially among newborns, for whom they usually produce asymptomatic infections; in older children and adults, these viruses likewise have a tendency to produce asymptomatic infections; although rarely fatal in well-nourished children, members of the genus *Rotavirus* are estimated to cause a million deaths every year in undernourished children.

Evasion of host defenses — avoids host immune defenses by infecting immune cells (genus *Coltivirus*), avoids host non-immune defenses by resistance to heat, low pH, and proteolytic attack (infectivity actually increased by proteolytic attack) (members of the genera *Orthoreovirus* and *Rotavirus*).

Predominant routes of transmission between hosts: Indirect (vehicle-borne) contact via fecally contaminated water, food, and fomites with the orthoreovirus possibly also being spread by aerosols.

R. Viral Family Retroviridae

Genera affecting humans: *BLV-HTLV retroviruses*, *Lentivirus*, *Spumavirus*.

Familial nature with respect to members affecting humans: Viruses of humans.

Alternate hosts: Species affecting humans seem naturally limited to humans.

Types of illnesses induced in humans: Carcinoma, encephalitis, leukemia (adult T-cell), lymphoma (adult T-cell), progressive chronic immunosuppression and immunodepletion (including acquired immunodeficiency syndrome), progressive myelopathy, sarcoma.

Familial strategies:

Infection course — productive, short term-initial, often followed by increasing to end-stage; also may seem nonproductive in the case of some endogenous retroviruses.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the immune cells (largely T-cell populations); secondary tissue and organ tropisms are toward the brain and intestines; at the host population level, those viruses considered transmissible (i.e., excluding endogenous retroviruses) have a very low transmissibility rate, produce infections whose incubation times are very long (10–40 years), and may pass through breast milk; the endogenous retroviruses are permanently integrated into the human genome and are passed genetically to all offspring.

Evasion of host defenses — avoids host immune defenses by rapid viral mutation and by infecting immune cells.

Predominant routes of transmission between hosts: Direct contact via host-to-host transfer of contaminated bodily fluids.

S. Viral Family Rhabdoviridae

Genera affecting humans: *Lyssavirus*, *Vesiculovirus*.

Familial nature with respect to members affecting humans: Zoonotic.

Natural hosts: Foxes, skunks, and vampire bats (genus *Lyssavirus*), cattle and horses (genus *Vesiculovirus*).

Types of illnesses induced in humans: Neuronal infections leading to encephalitis which appears invariably fatal (genus *Lyssavirus*); myalgia (genus *Vesiculovirus*).

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the neurons, including those in the spinal cord and limbic system of the brain, and the salivary glands (genus *Lyssavirus*); and toward either the muscles or nerves (genus *Vesiculovirus*); secondary tissue and organ tropisms are toward the adrenal cortex and pancreas (genus *Lyssavirus*); at the host population level, these viruses are essentially nontransmissible.

Evasion of host defenses — avoids host immune defenses by limited antigenic exposure within the host because the virus largely remains within neuronal cells until near end-stage (genus *Lyssavirus*).

Predominant routes of transmission between hosts: Direct contact via host-to-host contact associated with deposition of contaminated saliva into a bite wound and possibly associated with contamination of skin or mucosal wounds by other types of bodily fluids; in the case of the genus *Vesiculovirus*, vesicular fluids.

T. Viral Family Togaviridae

Genera affecting humans: *Alphavirus*, *Rubivirus*.

Familial nature with respect to members affecting humans: Viruses of human and zoonotic.

Natural or alternate hosts: Species of the genus *Alphavirus* cross-infect a wide variety of terrestrial vertebrates, mostly via mosquitoes and ticks; one species of the genus *Rubivirus* affects humans and it seems restricted to humans.

Types of illnesses induced in humans: Arthralgia, arthritis, diabetes, encephalitis, fetal developmental abnormalities (cardiological, diabetic, and neurological — including auditory, encephalitic, and visual — caused by *Rubivirus* if contracted during the first trimester of pregnancy), macular rash of skin, myalgia, myositis.

Familial strategies:

Infection course — productive, short term-initial.

Viral replication — at the individual host level, primary tissue and organ tropisms are toward the immune cells (specifically monocytes and macrophages in bone marrow, liver, lymph nodes, and spleen) and oropharynx; secondary tissue and organ tropisms are toward the beta cells of the pancreas, muscles, neurons of the central nervous system including the brain, skin, and synovial cells of joints; at the host population level, most members of the genus *Alphavirus* seem poorly transmitted between humans, and humans probably represent a dead-end host; infection by the genus *Rubivirus* is seldom fatal but highly transmissible via aerosols and usually causes a trivial exanthema of childhood or mild symptoms in adults, although infection during the first trimester of pregnancy can result in extremely severe developmental abnormalities.

Evasion of host defenses — avoids host immune defenses by infecting immune cells.

Predominant routes of transmission between hosts: Direct contact via either host-to-vector (genus *Alphavirus*), host-to-host (genus *Rubivirus*), or indirect (vehicle-borne) contact via aerosols (genus *Rubivirus*).

V. CONCLUSIONS

There are many types of viruses that afflict humans. We have managed to coevolve with some of these to lessen our misery. The struggle will continue as new viruses appear and as the existing ones reshuffle their genes or change their antigenicity by mutation. In the end, the contest is a struggle of biology versus biology, and the basic biology of the viruses is the same as ours.

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